It is known that iodine deficiency is a major cause of goiter development. However, there are many other causes that can lead to an increase and change in the consistency of the thyroid. In order to be able to come to an unambiguous assessment, differential diagnostic skills are essential. Therefore, the following article may help you learn more about the etiology and differential diagnosis of goiter.

Definition of Goiter

Goiter as a symptom
The term “goiter” is purely descriptive in nature and thus reveals nothing about the pathogenesis or the functional status of the thyroid gland. Therefore, goiter is a symptom. So, it primarily describes the enlargement of the thyroid and refers by means of other terms to the type and location of that very enlargement.

When talking about a goiter, we mean the thyroid gland exceeds the gender- and age-specific normal volume range. Women have a thyroid volume of more than 18 ml, men – a bit more than > 25 ml.

**Epidemiology of Goiter**

**Goiter — Common findings**

Thyroid enlargement and thyroid nodules are frequent findings in practice. Sonographically, 20 % of people at the age of 25 and 50 % of people over the age of 50 have a goiter. The prevalence of nodular thyroid abnormalities compounds 20 % more among individuals over 50 (Böhm 2009). Overall, women are more often affected than men.

**Classification of Goiter**

**Classification of goiter-size stages by WHO**
No goiter

Ia  Palpable goiter, not visible when bending the head back, solitary nodule
Ib  Palpable goiter, only visible when bending the head back
II  Visible and palpable goiter even without the inclination of the head
III Goiter visible at a distance, with obstruction of the trachea and esophagus or spreading behind the sternum

Classification of goiter after thyroid hormone function

<table>
<thead>
<tr>
<th>Euthyroid</th>
<th>Thyroid hormone level in the normal range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypothyroidism</td>
<td>Decreased thyroid hormone level</td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td>Increased thyroid hormone level</td>
</tr>
</tbody>
</table>

Etiology and Pathogenesis of Goiter

Multiple causes of goiter

The causes of goiter occurrence are manifold. The most common cause in industrialized countries is an **endemic iodine deficiency** (alimentary iodine deficiency). Other possible causes are:

**Inflammation**
- Immune thyreopathies (Graves’ disease, Hashimoto’s thyroiditis)
- Medications (phenytoin, lithium, anti-thyroid drugs, carbimazole)

**Thyroid autonomy**

**Thyroid tumors**
- Neoplastic production of TSH
- Acromegaly
Symptoms of Goiter

Non-specific symptoms as the first signs of goiter

Most goiters are asymptomatic. A visible thyroid enlargement can only be seen from a volume of about 40 ml. The enlargement of the thyroid can be accompanied with a mechanical impairment of organs and tissues bordering on it (tracheal and/or Esophagus compression).

The extent to which this goiter is symptomatic, essentially depends on its localization. In the case of retrosternal or retrotracheal growth, it may restrict the larynx and trachea in their anatomical position so much that dysphagia, dyspnea and hoarseness may occur.

In the case of esophagus compression, the patient complains about globus or pressure sensation in the throat, in addition to problems with swallowing.

<table>
<thead>
<tr>
<th>Common Symptom</th>
<th>Restricted Organ/Tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stridor, hoarseness, dyspnea</td>
<td>Compression of the trachea</td>
</tr>
<tr>
<td>Dysphagia, globus sensation</td>
<td>Compression of the larynx and/or trachea</td>
</tr>
<tr>
<td>Inflow congestion</td>
<td>Compression of the neck veins</td>
</tr>
</tbody>
</table>

Specific symptoms of goiter

Clear indications of the possible presence of goiter are diffuse or nodular changes of the thyroid tissue.

Diagnosis of Goiter

First signs of goiter

Avoiding necklaces, turtlenecks or an increase in the collar size can be regarded as the first indication of a goiter.

Anamnestically important questions in suspected goiter

A detailed medical history may provide the first evidence for the presence of a goiter. What should be questioned in detail:

- Duration and progression of thyroid enlargement
- Possible exposure of the head and neck region
- Recently occurred hoarseness
- Hormonal changes (puberty, pregnancy, menopause)
- Taking medications
- Iodine intake
- Family history
Goiter clinic

You should start with an examination. At the beginning of a first-glance examination, you may work with the goiter-size stages classification provided by WHO (see above). You should examine the thyroid with a straight back and a bowed head. You should pay attention to a possible visible enlargement as well as nodes and signs of upper inflow congestion.

Palpation stands in the foreground. During the physical examination, it allows making further judgment in regards to the extension of a goiter and other clinical signs of malignancy. Important in this case are:

- Mobility of the tissue;
- Any enlargement of the tissue;
- Uniform consistency of the tissue;
- Possibly, to palpate lumps and nodes;
- Buzz under the palpating fingers;
- Increased sensitivity to touch;
- Tenderness;
- Lymph node enlargement.

In addition to palpation, you may also use auscultation. If there is an increased blood supply to the thyroid tissue, this can be perceived as an audible buzz auscultation. If it happens, you should think of the presence of hyperthyroidism.

Further diagnosis in the presence of goiter

With a hardened anamnestic history and physical examination of the suspected goiter, the following examinations should take place:

- Ultrasonography of the thyroid for accurate detection of thyroid enlargement and morphological differentiation of the various forms of goiter.
- Determination of TSH, TRH, T3 and T4 for the evaluation of thyroid function.

Image: CT scanning and complete excision of giant thyroid goiter in posterior mediastinum. (A) Enhanced CT scanning reveals the right thyroid lobe (in red arrow) with a small cyst and a giant goiter (in blue arrow) in low
density on the back of the right lobe. (B) CT clavicle cross section reveals the giant goiter was located in the posterior mediastinum, compressing the trachea and esophagus. (C) CT of the chest reveals the goiter is well beyond the aortic arch and compressing the superior vena cava. (D) CT of the chest reveals the lower edge of the goiter reaches the carina of the trachea. (E) The tumor is in a complete capsule with large tension,” by Openi. License: CC BY 2.0

With a multinodular or nodular goiter, the following questions are to be answered: Is a thyroid autonomy available? Is it a benign change or a thyroid malignant tumor, if the tissues have changed? In order to get a differentiated answer to these questions, the following further diagnostic agents should be considered:

- Laboratory diagnostics;
- Scintigraphy;
- Unenhanced computed tomography;
- Magnetic Resonance Imaging;
- Fine-needle biopsy.

**Differential Diagnosis of Goiter**

**Various forms of goiter**

The diagnosis of goiter initially leads to the differentiation in **diffuse** and **nodular goiter**. However, among them we may subsume more different goiter forms with their conceptual assignment essentially depending on the nature of the change or the precise location of the thyroid tissue.

<table>
<thead>
<tr>
<th>Goiter Form</th>
<th>Description</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Euthyroid goiter (bland goiter)</td>
<td>Benign, with euthyroid serum levels and normal thyroid function.</td>
<td>With normal serum levels without direct clinical significance.</td>
</tr>
<tr>
<td>Euthyroid nodular goiter/ multinodular goiter</td>
<td>Nodular goiter, at the beginning mostly euthyroid; in the further course, there are signs of hyperthyroidism.</td>
<td>Hyperthyroidism</td>
</tr>
<tr>
<td>Diffuse goiter (struma parenchymatosa)</td>
<td>Not definable enlargement of the thyroid gland with uniform growth; common cause: iodine deficiency.</td>
<td>Puberty goiter, Graves’ disease</td>
</tr>
<tr>
<td>Basedow’s goiter</td>
<td>Diffuse parenchymal goiter with abundant vascular development, liquid colloid and epithelium tumor.</td>
<td>Graves’ disease</td>
</tr>
<tr>
<td>Lymphatic goiter Hashimoto (struma lymphomatosa Hashimoto)</td>
<td>Over the years, increasing focal or diffuse lymphocytic or plasma cellular infiltration of the thyroid, formation of lymphocytic follicles; final stage: fibrosis and disappearance of goiter parenchyma.</td>
<td>Hashimoto’s thyroiditis</td>
</tr>
<tr>
<td>Neonatal goiter</td>
<td>Thyroid enlargement in the newborn, endemic in iodine-deficient areas.</td>
<td>Goiter in the new-born</td>
</tr>
</tbody>
</table>

**Differential diagnosis of thyroid enlargement**

Main cause for the diffuse goiter is an alimentary iodine deficiency situation in industrialized countries. Consequence of this is a TSH-independent adaptive response in the sense of hyperplasia. If there is an enlarged thyroid, you have to think about a differential diagnosis:

- Diffuse goiter parenchymatosa;
Diffuse or colloid goiter;
- Hypertrophic Hashimoto’s thyroiditis;
- Graves’ hyperthyroidism;
- De Quervain’s thyroiditis;
- Invasive sclerosing thyroiditis (“Riedel’s thyroiditis”);
- Amyloidosis;
- Acromegaly.

Differential diagnosis of euthyroid nodular goiter

After noting a euthyroid nodular goiter (nodular goiter), possible malignant and inflammatory changes, as well as functional autonomies, have to be excluded. It should be included in the differential diagnosis in case of:

- Graves’ hyperthyroidism
- Functional autonomy (focal or disseminated)
- Malignant tissue changes (thyroid cancer)
- Hashimoto’s thyroiditis

Laboratory diagnosis of nodular and multinodular goiter

For the avoidance of medullary thyroid carcinoma (MTC), the determination of thyroid autoantibodies is recommended via sonographic examination of:

- Thyroid peroxidase antibodies (TPO antibodies) and
- TSH receptor antibodies (TRAB).
Other laboratory parameters to check the thyroid function are:

- Triiodothyronine (T3);
- Thyroxine (T4);
- Thyroid-stimulating hormone (TSH);
- Thyroid releasing hormone test (TRH test);
- Microscopic antibodies (MAbs);
- Thyroglobulin antibodies (TgAb).

**Differential diagnosis of multinodular goiter**

A particular challenge in the differential diagnosis of thyroid disease is a multinodular goiter. By means of sonography and scintigraphy, you should be able to identify suspicious focal or disseminated autonomies (a cold/hot node) and make further analysis. The aim of the examination is the detection or exclusion of thyroid autonomy.

If scintigraphically conspicuous nodes are detected, these require a further clarification, which, in turn, should take place by means of fine-needle biopsy. The main purpose of the fine-needle biopsy in this case is the selection of thyroid nodules for the earliest possible histological evaluation of clinically normal or malignant tumors (thyroid carcinoma).

**Differential Diagnosis of Throat Swelling**

Not every throat swelling is to be regarded automatically as a goiter. A throat swelling can also occur as part of an increase in the volume of parathyroid glands, salivary glands, lymph nodes and the skin, the blood vessels, the muscles and the skeletal system. The differential diagnosis takes the following specific causes into consideration:

<table>
<thead>
<tr>
<th>Possible Disease</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goiter</td>
<td>Frequently</td>
</tr>
<tr>
<td>Lymphadenopathy due to infections, sarcoidosis, lymphadenitis, etc.</td>
<td>Very often</td>
</tr>
<tr>
<td>Salivary gland swelling (tumor/stone/inflammation)</td>
<td>Less common</td>
</tr>
<tr>
<td>Thrombosis or tumor-related superior vena cava syndrome</td>
<td>Rarely</td>
</tr>
</tbody>
</table>

**Therapy of Goiter**

**Treatment of individual goiter forms**

Initially, the motto “wait and watch” should be applied with asymptomatic patients. Treatment is required only in case of complaints, a proven thyroid autonomy or well-secured malignancy.

However, if waiting is contraindicated, there is a possibility of drug treatment (levothyroxine, iodide). In addition, a radioiodine therapy or surgical therapy may be considered.

Still, each therapeutic procedure should be reviewed in terms of its sensibility prior to taking action. Thus, the majority of patients with a node first require no treatment, whereas, the treatment with malignancy is unquestionable. The thyroid surgery is obligatory for malignancy!

In the case of euthyroid diffuse goiter iodine deficiency is the main cause. Thus, the goal of any treatment should be the correction of intrathyroidal iodine deficiency.
In the case of retrosternal or mediastinal goiter expansion, with the impairment of adjacent organs of the respiratory and digestive tract, a thyroidectomy in the affected region should be considered.

**Important to Remember**

- Goiter is a symptom, not a disease.
- Initially, it indicates the enlargement of the thyroid.
- Rough classification of goiter: diffuse and nodular goiter types.

In case of a goiter suspicion, you should always exclude a possibly present malignancy.

**Evidence of a goiter** include:

- Thyroid enlargement;
- Nodules under the palpating fingers;
- Dysphagia;
- Dyspnea;
- Hoarseness;
- Difficulty swallowing, etc.

The examination of the eventually degenerated thyroid tissues occurs via sonography, scintigraphy and fine-needle biopsy.

In addition to goiter, further possible changes of the neck should be taken into consideration when a throat swelling is present. They may indicate entirely different diseases, such as swollen lymph nodes or the increase in the volume of salivary glands.

**Review Questions**

The answers are below the references.

1. A lack of iodine cannot result in:
   A. lowering of thyroid stimulating hormone (TSH) plasma concentration.
   B. reduction of triiodothyronine plasma concentration.
   C. thyroid enlargement (goiter).
   D. growth failure.
   E. disturbances of intellectual development.

2. Triiodothyronine (T3) and thyroxine (T4) hormones are formed in the thyroid. The precursor of these hormones is deposited extracellularly in the follicles from which the finished thyroid hormones are released by intracellular proteolysis. What is located in the follicles of the thyroid gland?
   A. Thyroglobulin
   B. Thyrotropin-releasing hormone (TRH)
   C. Iodate
   D. Thyroxine-binding globulin
   E. Transthyretin

3. Disorders in the synthesis of thyroid hormones and regulation of the thyroid function are associated with a variety of symptoms in children and adults. Hyperthyroidism can be caused by autoantibodies that are bound to receptors with the thyroid epithelial cells. Which receptors are activated by these
**autoantibodies?**

A. Somatostatin  
B. Thyreocalcitonin  
C. Thyroid-stimulating hormone (TSH)  
D. Thyreostatin  
E. Thyroliberin (TRH)

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**Correct answers:** 1A, 2A, 3C

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